

Case Report Section

Isolated 1q21 rearrangement der(20)t(1;20)(q21;p13) with telomere involvement of 20p in a case of longstanding myelodysplastic syndrome

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Abstract

Case report on Isolated 1q21 rearrangement der(20)t(1;20)(q21;p13) with telomere involvement of 20p in a case of longstanding myelodysplastic syndrome.

Clinics

Age and sex

58 years old male patient.

Previous history

No preleukemia; no previous malignancy; no inborn condition of note

Organomegaly

No hepatomegaly, no splenomegaly, no enlarged lymph nodes, no central nervous system involvement

Blood

WBC: 4.3X 10⁹/l

HB: 7.8g/dl

Platelets: 232X 10⁹/l

Blasts: 0%

Bone marrow: Bone marrow was hypercellular with erythroid hyperplasia (68% erythroid precursors) and erythroblastic and megakaryocytic dysplasia. The most typical dysplastic features in the erythroid line were the changes in nuclear morphology

(multinuclearity, nuclear hyperlobulation, irregular nuclear contours and karyorrhexis). Some of the erythroblasts resembled the blasts of the pure erythroid leukemia (large cells with deep cytoplasmic basophilia and oval nucleus with prominent nucleolus). The test of ring sideroblasts was positive (55%). Megakaryocytic dysplasia was present with hypo- or unilobulated megakaryocytes of all sizes. Micromegakaryocyte and dysplastic megakaryocytic fragments were also seen.

Cyto-Pathology Classification

Immunophenotype not done

Rearranged Ig Tcr not done

Pathology

The peripheral blood morphology was characterized with poikilo anisocytosis and presence of single oxyphilic erythroblasts. Differential blood count was 1% myelocytes, 2% metamyelocytes, 32% bands, 27% segments, 20% lymphocytes, 17% monocytes and 1% eosinophils.

Electron microscopy not done

Diagnosis

Refractory cytopenia with multilineage dysplasia and ring sideroblasts.

Note

The patient was hospitalized for the first time in January 2006 with two years history of mild anemia. The examinations showed: Hb 104 g/dl, WBC $5 \times 10^9/l$ and platelets $327 \times 10^9/l$. Bone marrow was hypercellular with dysplasia of the erythroid lineage presented with megaloblastic erythropoiesis. Conventional cytogenetic analysis revealed a karyotype of 46, XY,der(20)t(1;20)(q21;p13)[20]. The diagnosis of refractory anemia was made and the patient was followed-up until 2015. In this period the patient was in a good clinical condition and good quality of life maintaining hemoglobin value between 95 -120 g/dl without blood transfusions. In October 2015 the patient was hospitalized again. Conventional and molecular cytogenetic analyses confirmed the karyotype of 46,XY,der(20)t(1;20)(q21;p13). The diagnosis of refractory cytopenia with multilineage dysplasia and ring sideroblasts was made and the patient received supportive treatment with blood transfusions. In February 2016 the disease progressed to a refractory anemia with excess of blasts-2 (14% myeloblasts in bone marrow) and one course of chemotherapy with low doses of Cytarabine (80 mg daily) was carried out. The patient was followed-up in a satisfactory clinical condition maintaining hemoglobin value between 75 and 80 mg/ml and myeloblasts in the bone marrow between 2% and 4%.

Survival

Date of diagnosis 01-2006

Treatment

Blood transfusions and chemotherapy with low doses of Cytarabine.

Complete remission: no

Treatment related death: no

Relapse: no

Status Alive

Last follow up 03-2017

Survival

138 In March 2017 peripheral blood showed WBC $4.3 \times 10^9/l$, Hb 65 g/dl, platelets $175 \times 10^9/l$ and differential blood count 1% metamyelocytes, 5% bands, 52% segments, 31% lymphocytes, 6% monocytes and 5% eosinophils. Bone marrow examination revealed normocellular marrow with trilineage dysplasia and 4% blasts.months

Karyotype

Sample Bone marrow

Culture time 24h

Banding GTG banding.

Results

46,XY,der(20)t(1;20)(q21;p13)[33].

The conventional cytogenetic study revealed karyotype of 46,XY,der(20)t(1;20)(q21;p13)[33] (Fig. 1A).

This unbalanced translocation resulted in the formation of a derivative chromosome, composed of the recipient chromosome 20 and the additional copy of 1q21->qter: der(20)(1qter->1q21::20p13->20qter). In some metaphases the translocated segment 1q21qter is as though attached to an intact chromosome 20, suggesting that the breakpoint in 20p is sub-telomeric or telomeric (Fig.1A).

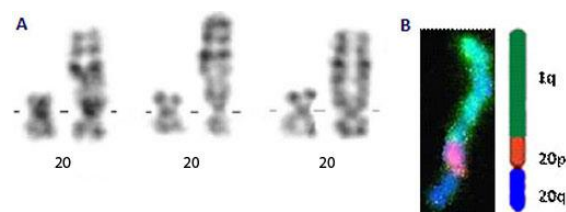


Figure 1. (A) Partial G- banded karyotypes demonstrating derivative chromosome 20. (B) fluorescence 'in situ' hybridization of the derivative chromosome 20 with arm specific probe for 1q and 20p compared with the respective schematic model of its structure.

Other molecular cytogenetics technics

FISH examinations were carried out according to manufacturer's instructions, using arm specific probes for 1q (ASP1q) and 20p (ASP20p), sub-telomere DNA probe for 20p (Kreatech Diagnostic, Leica, Germany) and telomere probe for 20p (Vysis/Abbott Molecular, Des Plaines, IL, USA). Sub-telomere DNA probe was applied independently and in combination with the arm specific probes for 1q. Images were captured and analyzed with epifluorescent microscope Nikon 80i (Nikon corporation, Tokyo, Japan) equipped with CCD camera and DAPI/red/green filter set.

Other molecular cytogenetics results

FISH examination with ASP1q and ASP20p probes and combination of sub-telomere DNA probe with ASP for 1q showed normal sub-telomere confirmed the 1q trisomy and demonstrated that the additional copy of 1q21qter was translocated to the short arm of chromosome 20 (Fig 1B and 2A).

In two of the 55 metaphases analyzed der(20) was not present. One was with trisomy and the other one with tetrasomy of chromosome 1. FISH examination with both sub-telomere and telomere DNA probes for 20p showed normal sub-telomere and telomere signal patterns - ish der(20)t(1;20)(q21;p13)(D20S1156x2) and ish der(20)t(1;20)(q21;p13)(D20S1157x2) (Fig 2B, 2C and 2D).

Other Molecular Studies

Technics:

Microarray examination of the patient's bone marrow DNA was performed with CGH+SNP 60K microarray platform (OGT, Oxford, UK) according to the manufacturer's protocol. The hybridization of the reference and patient's DNA was made via incubation in Mai-Tai hybridization system (SciGene, USA) for 22-hours at 65°C. Slides were scanned using scanner GenePix 4400A (Molecular Devices, USA) and features were extracted by GenePixPro7 software (Molecular Devices, USA). The microarray patient's profile was analysed with CytoSure Interpret software, v 4.4.6. (OGT, Oxford, UK) using HG 19.

Results:

aCGH study found only the gain of the segment 1q21qter and revealed no 20p losses - arr[hg] 1q21.1q44(142,706,628-248,514,266)x3 (Fig.3 D and C). Both aCGH and FISH study with sub-telomere and telomere probes indicated that the breakpoint in the derivative chromosome 20 is located in the telomere region.

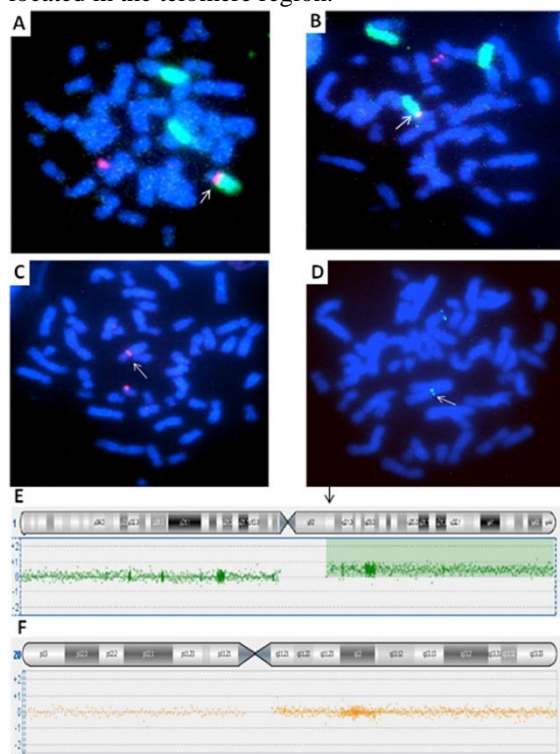


Figure 2. (A) Metaphase fluorescence "in situ" hybridization with arm specific probe for 1q (green signal) and 20p (red signal) demonstrating the translocation of the additional copy of 1q21qter to the short arm of chromosome 20. (The derivative chromosome 20 is arrowed). (B) Fluorescence "in situ" hybridization with arm specific probe for 1q (green signal) and 20p sub-telomere probe (red signal) showing two normal signals: one in the normal chromosome 20 and one fitting tightly to the additional copy of 1q21qter (arrowed). (C) Metaphase fluorescence "in situ" hybridization with 20p sub-telomere probe demonstrating two normal signals - one in the normal and one in the derivative chromosome 20 (arrowed). (D) Metaphase fluorescence "in situ" hybridization with 20p telomere probe demonstrating two normal signals - one in the normal and

one in the derivative chromosome 20 (arrowed). (E) Ideogram and microarray CGH plot of chromosome 1 showing a gain for the segment 1q21-qter (green shaded area; the breakpoint is arrowed). (F) Ideogram and microarray CGH plot of chromosome 20 showing no deletion on the p-arm.

Comments

Der(20)t(1;20)(q21;p13) belongs to the group of the unbalanced 1q12-21 translocations observed mostly as a second genetic event in a large spectrum of hematological malignances (Zamecnikova A and Al, Bahar S. 2013). Unbalanced 1q12-21 translocations affecting 20p have been reported in 10 cases: 6 with multiple myeloma (Fiedler et al., 1992; Taniwaki et al., 1994; Keung et al., 1998; Sawyer et al., 1998; Mohamed et al., 2007; Sawyer et al., 2014), 1 with acute lymphoblastic leukemia/ lymphoblastic lymphoma (Wan et al., 2004), 1 with diffuse large B-cell lymphoma (Levine et al., 1985), 1 with acute myeloid leukemia (M7) (Yoshida et al., 2013) and 1 with chronic myeloproliferative disorder (L'Abbate et al., 2015). The molecular pathogenesis of *der(20)t(1;20)(q12-21;p13)* is linked to the gain of 1q and the losses of coding DNA from 20p. The presented case demonstrated that the breakpoint in 20p could occur in telomere region as were reported in other 1q translocations: 3 with *der(2)t(1;2)(q12-21;q37)*, 2 with *der(16)t(1;16)(q12-21;q24)* (Busson-Le Coniat M et al., 1999) and 1 with *der(12)t(1;12)(q21;p13)* (La Starza R et al., 1999). Because of the telomere involvement of the recipient chromosomes these 1q12-21 translocations did not result in losses of coding DNA and their molecular pathogenesis is possibly linked only to the gain of 1q. We supposed that in our case the missing of 20p losses as well as additional anomalies in the karyotype are the reasons for the long survival of the patient.

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